

Substitute Specification – Clean Version

What is claimed is:

1. A pharmaceutical composition for transmucosal administration of an exendin or exendin analog, comprising an exendin or an exendin analog, a cationic polyamino acid, and a buffer; wherein at the pH of the composition the buffer does not cause precipitation of the cationic polyamino acid and has a mono-anionic or neutral net charge; and wherein the transmucosal absorption of the exendin or exendin analog is increased relative to the absorption of the exendin or exendin analog in the absence of the polyamino acid.
- 5 2. The composition of claim 1, wherein the pH of the composition is between about pH 4.0 and about pH 6.0.
3. The composition of claim 1, wherein the pH of the composition is between about pH 4.0 and pH 5.0.
4. The composition of claim 1, wherein the buffer is selected from the group consisting of acetic acid, ϵ -aminocaproic acid or glutamic acid.
5. The composition of claim 1, wherein the buffer comprises glutamic acid.
6. The composition of claim 1, further comprising a tonicifying agent, a viscosity-increasing agent, a bioadhesive agent, a preservative, or any combination thereof.
7. The composition of claim 1, wherein the cationic polyamino acid comprises poly-histidine, poly-arginine, poly-lysine, or any combination thereof.
8. The composition of claim 7, wherein the cationic polyamino acid has an average molecule weight of between about 10 kDa and about 200 kDa.
9. The composition of claim 1, wherein the exendin or exendin analog is selected from at least one of the group consisting of exendin-3, exendin-4, exendin-4 acid,

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exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, ¹⁴Leu, ²⁵Phe exendin-4 amide, and ¹⁴Leu, ²⁵Phe exendin-4 (1-28) amide.

10. The composition of claim 1, wherein the exendin or exendin analog comprises exendin-4.

11. The composition of claim 1, wherein the exendin or exendin analog comprises exendin-3.

12. The composition of claim 1, wherein the exendin or exendin analog comprises at least one exendin selected from the group consisting of SEQ ID NOs: 9-39, 187 and 188.

13. The composition of claim 1, wherein the exendin or exendin analog comprises at least one exendin or exendin analog selected from the group consisting of SEQ ID NOs: 6-8 and 40-186.

14. The composition of claim 1, wherein the exendin or exendin analog comprises an amino acid sequence according to SEQ ID NO. 3.

15. The composition of claim 1, wherein the exendin or exendin analog comprises an amino acid sequence according to SEQ ID NO. 4.

16. The composition of claim 1, wherein the exendin or exendin analog comprises an amino acid sequence according to SEQ ID NO. 5.

17. The composition of claim 6, wherein the tonicifying agent is selected from the group consisting of sodium chloride, mannitol, sucrose, glucose and any combination thereof.

18. The composition of claim 6, wherein the viscosity-increasing agent is selected from the group consisting of hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose of average molecular weight between about 10 and about 1,500 kDa, starch, gums, and any combination thereof.

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19. The composition of claim 6, wherein the bioadhesive agent is selected from the group consisting of carbomer, polycarbophil and any combination thereof.
20. The composition of claim 6, wherein the preservative is selected from the group consisting of phenylethyl alcohol, methylparaben, ethylparaben, propylparaben, butylparaben, chlorbutanol, benzoic acid, sorbic acid, phenol, m-cresol, alcohol, and any combination thereof.
21. The composition of claim 1, wherein the absorption is increased at least 2 fold.
22. The composition of claim 1, wherein the absorption is increased at least 5 fold.
23. The composition of claim 1, wherein the absorption is increased at least 10 fold.
24. A pharmaceutical composition for transmucosal administration of an exendin or an exendin analog comprising about 0.10% to about 5.0% (w/v) of an exendin or an exendin analog; about 0.01% to about 1.0% (w/v) of a cationic polyamino acid having a molecular weight between about 10 kDa and about 200 kDa; about 0.01% to
5 about 10.0% (w/v) of a buffer, wherein at a pH of between about 4.0 and 5.0, the buffer does not cause precipitation of the cationic polyamino acid and the buffer has a mono-anionic or neutral net charge; and wherein the transmucosal adsorption of the exendin or exendin analog is increased relative to the adsorption of the exendin or exendin analog in the absence of the cationic polyamino acid.
25. The composition of claim 24, wherein the exendin or exendin analog comprises exendin-4.

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26. A method for transmucosal administration of an exendin or an exendin analog comprising contacting a mucosal surface with a composition comprising an exendin or an exendin analog, a cationic polyamino acid, and a buffer for a time sufficient for a therapeutically effective amount of said exendin or exendin analog to pass through the mucosal surface; wherein at the pH of the composition, the buffer does not cause precipitation of the cationic polyamino acid and the buffer has a mono-anionic or neutral net charge; and wherein the transmucosal adsorption of the exendin or exendin analog is increased relative to the absorption of the exendin or exendin analog in the absence of the cationic polyamino acid.
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27. The method of claim 26, wherein the exendin or exendin analog comprises exendin-4.